AMENDMENTS TO THE DRAWINGS

The attached two sheets of drawings include changes to FIGS. 4 and 5. These sheets, which include FIGS. 3-5, replace the original two sheets including FIGS. 3-5. In FIGS. 4 and 5 the AcO group on the lactone reactant has been deleted.

Attachments: 2 Replacement Sheets

2 Annotated Sheets

REMARKS

Claims 11-27 are pending. Claims 13-20 are withdrawn as not elected. Claims 11, 12, and 21-27 are rejected.

AMENDMENT TO THE DRAWINGS

FIGS. 4 and 5 are amended to correct a typographical error. The amendment removes the acetoxy groups in the lactone reactant in each of FIGS. 4 and 5. The acetoxy group was inadvertently included in these reactants. The correction is supported at least at p. 16 line 15 to p. 17 line, which describes a lactone, not an acetoxy lactone:

> A typical preparation of an azidoxanthone derivative is outlined in FIG. 4. The acid chloride is reacted with the lactone under Friedel-Crafts conditions to give the benzophenone intermediate, which is saponified and cyclized at once to the nitroxanthone. The nitro group is then converted to the azide by a standard sequence of reactions, that is, reduction, diazotization, and sodium azide treatment. The lactone ring should be sufficiently reactive for conjugation to biomolecules mentioned previously.
>
> Azidoanthraquinone derivatives can be synthesized according to FIG. 5. The diacid chloride is reacted with the lactone under Friedel-Crafts conditions to the corresponding nitroanthraquinone. The nitrogroup is then converted to the azido group by the standard procedure previously described. The lactone ring is sufficiently reactive for conjugation to the desired biomolecule or, alternatively, it could be hydrolyzed to the acid and then coupled to the biomolecule by conventional methods.

In addition, the products of each of FIGS. 4 and 5 are not produced unless the acetoxy group is omitted Thus, no new matter is introduced and Applicants respectfully request the correction be made.

CLAIM REJECTIONS UNDER 35 U.S.C. §112

Claims 11, 12, and 21-27 are rejected under 35 U.S.C. §112 ¶1 as not described.

In reference to the list of "bombesin receptor binding molecule" discussed in Applicants' March 14, 2008 Amendment, the Examiner's position is that there is no support in the specification and that the specification did "little more than outline goals appellants hope the claimed invention achieved and the problems the invention will hopefully ameliorate"; that the "description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention"; and

> mere indistinct terms (such as various "receptor binding molecules" used herein), however may not suffice to meet the written description requirement" as per Univ. of Rochester v. G.D. Searle, in that "A description of what a material does, rather than of what it is, usually does not suffice...The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described.

The Examiner states that

> the claims are directed to a compound where E is selected from various receptor binding molecules. There is no structural information provided in the specification to teach what structure is required to meet the stated function. It appears from the drawing that two possible receptors are

> shown. There may be more incorporated by reference, but that results in a very limited number of receptor binding molecules which do not share common structures which would allow one of ordinary skill to understand the term receptor binding molecule. As such, one of ordinary skill in the art would not understand the structural requirements based on the general binding functionality language.

The claimed method recites a phototherapeutic procedure using the recited compound E - L - Ar - X - N_3. N_3 is the azide moiety that produces nitrene upon photoactivation. Ar is a chromophore that undergoes sensitization. L is a linker between Ar and E. E is a group that targets the compound to a particular body site where phototherapy is needed; as disclosed, E may not be required.

> For targeting purposes, external attachment of an epitope is used. If the aromatic azido compounds themselves preferentially accumulate in the target tissue, however, an additional binding group may not be needed. For example, if Ar is an anthracycline moiety, it will bind to cancer cells directly and not require an epitope for targeting purposes. p. 9 lines 8-12

In the previous Action, the Examiner queried how or even if the biomolecule will attach to a CH_2 group. Applicants response included an inventor's Declaration under 37 C.F.R. explaining the chemical reactions.

Responsive to the current rejections, Applicants herein submit a second Declaration under 37 C.F.R. §1.132, from an independent third-party, addressing the Examiner's specific issues, namely, that a person of ordinary skill in the art would know (1) the identity of a "bombesin receptor binding molecule" by structure as well as by function; (2) whether and where a "receptor binding molecule" would attach to a methene group; (3) whether the receptor binding molecule must have a peptide chain; and (4) if it did not have a peptide chain, how the receptor binding molecule would bind.

The Declarant analyzes how structures of "bombesin receptor binding molecules" are known (e.g., bombesin, bombesin agonists, and bombesin antagonists), and whose structures are known or readily determined, without undue experimentation, by a person of ordinary skill in the art. The Declarant analyzes that such a binding molecules would attach to a methene group by a nucleophilic displacement reaction. The Declarant describes both the peptide nature of known bombesin receptor binding molecules, and the possibility of conjugating a non-peptide compound to a peptide using conjugation chemistry techniques known to a person of ordinary skill in the art.

Applicants assert that the claims meet the requirements under 35 U.S.C. §112 ¶1. Adequacy of disclosure is judged from the perspective of one of ordinary skill in the art; to this end, Applicants now have submitted two Declarations under 37 C.F.R. §1.132 demonstrating adequate description. Written description does not contain a length requirement, nor are examples, actual reduction to practice, or recitation of structure of a biological macromolecule required. *Falkner v. Inglis* 79 USPQ2d 1001 (Fed. Cir. 2006).

Should the Examiner fault these Declarants' statements, Applicants respectfully request the specificity and supporting affidavit, as permitted under 37 C.F.R. §1.104(d)(2):

> When a rejection in an application is based on facts within the personal knowledge of an employee of the Office, the data shall be a specific as possible, and the reference must be supported, when called for by the applicant, by the affidavit of such employee, and such affidavit shall be

> subject to contradiction or explanation by the affidavits of the applicant and other persons.

For at least these reasons, Applicants assert that the public is put in possession of the invention, and that there is sufficient detail so that a person of ordinary skill in the art can reasonable conclude that the inventors had possession of the invention, as required for written description, and respectfully request the rejection be withdrawn.

CLAIM REJECTIONS UNDER 35 U.S.C. §102

Claim 11 is rejected under 35 U.S.C. §102(b) as anticipated by Pinney.

The Examiner states

> Pinney et al discloses the use of aryl azides as potent antiestrogens, such as LY117018 and LY139481 (page 2422, 2nd full paragraph and images at the top right corner). The attachment is at the estrogen receptor (page 2422 first few lines). Note, the instant compound may be attached through L as –(CH2)a-, where a can be 0 and X is –(CH2)h- where h is 0.

Applicants' have amended claim 11 to exclude a = 0 when L = -$(CH_2)_a$ and E = steroid binding molecule, or h = 0 when X = $(CH_2)_h$- and E = steroid binding molecule.

Applicants respectfully assert that the rejection has been overcome and requests its withdrawal.

CLAIM REJECTIONS UNDER 35 U.S.C. §103(a)

Claims 11, 12, and 21-27 are rejected under 35 U.S.C. §103(a) as obvious over Sykes U.S. Patent No. 6,313,274 in view of Pinney.

The Examiner states (citations omitted):

> Sykes et al teaches phototherapeutic treatment using the protein somatostatin. Proffered administration is via injection. Sykes also teach the use of arylazides as photoactivatable agent.
>
> Sykes does not teach the attachment of aryl azides as part of phototherapy.
>
> Pinney et al teaches the addition of an aryl azide enhances the reactivity of the nitrene generated upon photolysis when using receptor binding molecules. Pinney et al further teaches 30 nM fully saturate the ER sites.
>
> Pinney et al does not teach the use [*sic*] protein somatostatin as the receptor binding molecule.
>
> It would have been obvious to one of ordinary skill in the art to recognize that when practicing the method of the primary reference, that the addition of an aryl azide as taught by the secondary reference will improve the performance of the method. Therefore the combination would be an obvious improvement of the therapy taught in the primary reference.

Applicants respectfully disagree. Sykes teaches the use of photoactivable agents, including arylazides, only to immobilize an antigen or antibody on a support.

> Photoactivable agents, including arylazides, have been used to immobilize an antigen or antibody on a support (Sykes col. 2 lines 47-48).

Sykes teaches away from any other use of the photoactivable agent, such as Applicants' use to effect therapy. This is because Sykes' teaches that photoactivation of an arylazide will affect the properties of the antigen or antibody, therefore, Sykes omits an arylazide (Sykes col. 5 lines 10-26, distinguishing Noujaim).

Thus, Sykes does not teach, suggest, or motivate that arylazide is part of a compound that can be used for phototherapy, hence, it does not render Applicants' method obvious.

Because the primary reference fails, the secondary reference cannot stand. Thus, the basis of the Examiner's rejection, that one of ordinary skill in the art would recognize that the addition of an aryl azide will improve the performance of the method, is not proper because Sykes, the primary reference, does not teach Applicants' method.

Applicants thus respectfully request that the rejection be withdrawn.

CONCLUSION

The application is believed to be in condition for allowance. Payment of the fee for a one-month extension is made simultaneously herewith by Electronic Funds Transfer. The Office is authorized to charge any fee deficiency, or credit any overpayment, to Deposit Account No. 20-0809.

The Examiner is invited to contact Applicants' undersigned representative with questions.

Respectfully submitted,

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